Changes in **methylation** patterns identified by two-dimensional DNA fingerprinting.
1999

5/6/2 (Item 1 from file: 34)
10082932 Genuine Article#: 482XC Number of References: 53
Title: Dynamic impact of **methylation** at the M. HhaI target site: A solid-state deuterium NMR study (ABSTRACT AVAILABLE)
Publication date: 20011016

5/6/3 (Item 2 from file: 34)
06009503 Genuine Article#: XN918 Number of References: 39
Title: State of **methylation** of the human osteocalcin gene in bone-derived and other types of cells (ABSTRACT AVAILABLE)
Publication date: 19970901

5/6/4 (Item 1 from file: 98)
03253314 H.W. WILSON RECORD NUMBER: BGSI96003314 (USE FORMAT 7 FOR FULLTEXT)
The human genome: organization and evolutionary history.
WORD COUNT: 12668
'95 (19950000)
? t s5/7/1
>>>Format 7 is not valid in file 143

5/7/1 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

12073218 BIOSIS NO.: 199900368067
Changes in **methylation** patterns identified by two-dimensional DNA fingerprinting.
AUTHOR: Uhlmann Karen; Marczinek Karola; Hampe Jochen; Thiel Gundula; Nuernberg Peter(a)
AUTHOR ADDRESS: (a)Institut fuer Medizinische Genetik, Universitaetsklinikum Charite, D-10098, Berlin**Germany
JOURNAL: Electrophoresis 20 (8):p1748-1755 June, 1999
ISSN: 0173-0835
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: Two-dimensional DNA fingerprinting (**2-D** fingerprinting) is a sensitive tool for genomic difference analysis between tumor DNA and constitutive DNA of glioma patients. Numerous differences were found even in low-grade gliomas. They can be interpreted as deletions, amplifications, rearrangements, HaeIII **restriction** site mutations, tandem repeat instabilities, or **methylation** differences. The influence of methyl groups on the melting behavior of double-stranded DNA fragments in a denaturing gradient gel was demonstrated by analyzing the migration of lambda-phage DNA fragments in **2-D** fingerprint gels. A characteristic intensity shift between two neighboring spots in several glioma samples was identified and verified by rehybridization of **2-D** filters with a cloned DNA fragment corresponding to the lower spot in 10 out of 11 pilocytic astrocytomas. We hypothesized that this shift may be related to an alteration in the **methylation** pattern of the tumor DNA. This was specifically tested by analyzingthe underlying 750 bp genomic fragment (including 21 **CpG** dinucleotides) with bisulfite treatment of agarose-embedded DNA. A **methylation** grade of 88% in tumor DNA as

compared to 96% in blood DNA was found. Although only one **CpG** is located in the melting domain of the cloned fragment, this particular **CpG** is **methylated** in all blood samples, but mostly demethylated in the tumor samples. In conclusion, we demonstrate that **2-D** fingerprinting may be a powerful tool for the detection of DNA **methylation** changes in genomic difference analysis.

```
? s (restriction (w) landmark (w) genome (w) scanning)
          559250  RESTRICTION
           15078  LANDMARK
          519766  GENOME
          855404  SCANNING
      S6     169  (RESTRICTION (W) LANDMARK (W) GENOME (W) SCANNING)
? rd s6
...examined 50 records  (50)
...examined 50 records  (100)
...examined 50 records  (150)
...completed examining records
      S7      63  RD S6 (unique items)
? t s7/6/1-63
```

The detection of regions of aberrant DNA methylation in chronic myeloid leukaemia by **Restriction Landmark Genome Scanning** (RLGS).

...ABSTRACT: has been proposed that methylation-induced gene silencing may mediate the discordant maturation characteristic of **malignant** cells. In CML, the development of a number of hypermethylated regions, which precede blastic transformation...

...CML as a possible mechanism through which disease development may be mediated. The technique of **Restriction Landmark Genome Scanning** (RLGS) allows for the rapid assessment of multiple CpG sites within the DNA genome. It...
METHODS & EQUIPMENT: **restriction landmark genome scanning--**

8/KWIC/2 (Item 2 from file: 5)
DIALOG(R)File 5:(c) 2002 BIOSIS. All rts. reserv.

...gene for the axonal cell adhesion molecule TAX-1 is amplified and aberrantly expressed in **malignant** gliomas.

...ABSTRACT: chromosome 1 that has been implicated in microcephaly and the Van der Woude syndrome. Using **restriction landmark genome scanning** to search for amplified genes in gliomas, we found TAX-1 to be amplified in...
DESCRIPTORS:
DISEASES: **malignant** glioma...

8/KWIC/3 (Item 3 from file: 5)
DIALOG(R)File 5:(c) 2002 BIOSIS. All rts. reserv.

MISCELLANEOUS TERMS: ...**MALIGNANT** MELANOMA...

...**RESTRICTION LANDMARK GENOME SCANNING**

8/KWIC/4 (Item 1 from file: 144)
DIALOG(R)File 144:(c) 2002 INIST/CNRS. All rts. reserv.

English Descriptors: Human; Case study; Repeated sequence; Demethylation; Postoperative; Relapse; Recurrence; Prognosis; Hepatocellular carcinoma; Carcinogenesis; **Restriction landmark genome scanning**
Broad Descriptors: Hepatic disease; Digestive diseases; **Malignant** tumor; Foie pathologie; Appareil digestif pathologie; Tumeur maligne; Higado patologia; Aparato digestivo patologia; Tumor maligno

8/KWIC/5 (Item 2 from file: 144)
DIALOG(R)File 144:(c) 2002 INIST/CNRS. All rts. reserv.

English Descriptors: Human; Case study; Postoperative; Recurrence; Genetic marker; Carcinogenesis; Hepatocellular carcinoma; **Restriction landmark genome scanning**
Broad Descriptors: **Malignant** tumor; Hepatic disease; Digestive diseases; Tumeur maligne; Foie pathologie; Appareil digestif pathologie; Tumor maligno; Higado...

8/KWIC/6 (Item 3 from file: 144)

DIALOG(R)File 144:(c) 2002 INIST/CNRS. All rts. reserv.

English Descriptors: Squamous cell carcinoma; Oral cavity; Alteration; DNA; Technique; Molecular biology; Exploration; Pathogenesis; Human; Biopsy; **Restriction landmark genome scanning**
Broad Descriptors: Stomatology; Oral cavity disease; **Malignant** tumor; Stomatologie; Cavite buccale pathologie; Tumeur maligne; Estomatologia; Cavidad bucal patologia; Tumor maligno

8/KWIC/7 (Item 1 from file: 155)
DIALOG(R)File 155:

The underlying basis of the **malignant** progression of astrocytomas is a specific and cumulative series of genetic alterations, most of which ...

... the methylation status of 1,184 genes in each of 14 low-grade astrocytomas using **restriction landmark genome scanning** (RLGS). The results showed nonrandom and astrocytoma-specific patterns of aberrantly methylated genes. We estimate ...
? t s8/7/1-7
>>>Format 7 is not valid in file 143

8/7/1 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
(c) 2002 BIOSIS. All rts. reserv.

13098936 BIOSIS NO.: 200100306085
The detection of regions of aberrant DNA methylation in chronic myeloid leukaemia by **Restriction Landmark Genome Scanning** (RLGS).
AUTHOR: Davies C S(a); Plass C; Smiraglia D; Burnett A K(a); Mills K I(a)
AUTHOR ADDRESS: (a)Haematology, University of Wales College of Medicine, Cardiff**UK
JOURNAL: Blood 96 (11 Part 1):p350a November 16, 2000
MEDIUM: print
CONFERENCE/MEETING: 42nd Annual Meeting of the American Society of Hematology San Francisco, California, USA December 01-05, 2000
SPONSOR: American Society of Hematology
ISSN: 0006-4971
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: Aberrant DNA methylation in the promoter region of the genome has been shown to have profound effects on gene transcription. As such, it has been proposed that methylation-induced gene silencing may mediate the discordant maturation characteristic of **malignant** cells. In CML, the development of a number of hypermethylated regions, which precede blastic transformation, have been described. We describe the investigation of abnormal DNA methylation in chronic phase CML as a possible mechanism through which disease development may be mediated. The technique of **Restriction Landmark Genome Scanning** (RLGS) allows for the rapid assessment of multiple CpG sites within the DNA genome. It uses methylation sensitive restriction enzymes and a high-resolution 2-dimensional gel electrophoresis system to produce highly reproducible patterns from which changes in DNA methylation can be identified. We investigated the methylation status of the DNA genomes of five patients at disease presentation in chronic phase (CP). A number of genomic loci displaying abnormal methylation were detected, two of which, namely the trp-185 gene and the 28S ribosomal RNA gene, consistently displayed patterns of hypermethylation (5/5 and 4/5 patients

respectively). The prevalence of methylation changes at these regions was investigated further in a larger patient cohort using Sodium Bisulphite Modification and Methylation Specific PCR. This showed hypermethylation of the trp185 gene in CML was a highly significant event ($p<0.001$). Subsequent analysis of sequential samples showed that these methylation changes were stably inherited. As trp185 has a functional role in RNA expression, the methylation and the resulting block in gene expression may play a role in the onset of CML. In summary, this study highlights the occurrence of aberrant DNA methylation in CP-CML and suggests that abnormal methylation events are not exclusive to the blast crisis. This study confirms aberrant DNA methylation as a possible mechanism through which CML development and manifestation may be mediated.

8/7/2 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

12977650 BIOSIS NO.: 200100184799
The gene for the axonal cell adhesion molecule TAX-1 is amplified and aberrantly expressed in **malignant** gliomas.
AUTHOR: Rickman David S; Tyagi Rachana; Zhu Xiao-Xiang; Bobek Miroslav P; Song Suzan; Blaivas Mila; Misek David E; Israel Mark A; Kurnit David M; Ross Donald A; Kish Phillip E; Hanash Samir M(a)
AUTHOR ADDRESS: (a)Comprehensive Cancer Center, University of Michigan, A520 MSRB I, Ann Arbor, MI, 48109: shanash@umich.edu**USA
JOURNAL: Cancer Research 61 (5):p2162-2168 March 1, 2001
MEDIUM: print
ISSN: 0008-5472
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: The human TAX-1 gene encodes a Mr 135,000 glycoprotein that is transiently expressed on the surface of a subset of neurons during development and is involved in neurite outgrowth. The TAX-1 gene has been mapped to a region on chromosome 1 that has been implicated in microcephaly and the Van der Woude syndrome. Using **restriction landmark genome scanning** to search for amplified genes in gliomas, we found TAX-1 to be amplified in 2 high-grade gliomas among a group of 26 gliomas investigated. Real-time reverse transcription-quantitative PCR analysis detected high levels of TAX-1 mRNA in glial tumors, even in the absence of TAX-1 gene amplification. Immunohistochemical analysis revealed abundant levels of TAX-1 in neoplastic glial cells of glioblastoma multiforme tumors. Because glial tumors are highly invasive and in view of the role of TAX-1 in neurite outgrowth, we investigated the potential role of TAX-1 in glioma cell migration. Using an in vitro assay, we found that the migration of glioma tumor cells is profoundly reduced in the presence of either an anti-TAX-1 antibody or a TAX-1 antisense oligonucleotide. Our findings suggest that TAX-1 plays a role in glial tumorigenesis and may provide a potential target for therapeutic intervention.

8/7/3 (Item 3 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

09954250 BIOSIS NO.: 199598409168
Demethylation of a repetitive DNA sequence in human cancers.
AUTHOR: Miwa Wataru; Yashima Kazuo; Sekine Teruaki; Sekiya Takao(a)
AUTHOR ADDRESS: (a)Oncogene Div., Natl. Cancer Cent. Res. Inst., 1-1 Tsukjii 5-chome, Chu-ku, Tokyo 104**Japan

JOURNAL: Electrophoresis 16 (2):p227-232 1995
ISSN: 0173-0835
DOCUMENT TYPE: Article
RECORD TYPE: Citation
LANGUAGE: English

8/7/4 (Item 1 from file: 144)
DIALOG(R)File 144:Pascal

15685154 PASCAL No.: 02-0392093
Correlation of postoperative recurrence in hepatocellular carcinoma with demethylation of repetitive sequences
ITANO Osamu; UEDA Masakazu; KIKUCHI Kiyoshi; HASHIMOTO Osamu; HAYATSU Shigeo; KAWAGUCHI Masaharu; SEKI Hiroaki; AIURA Kouichi; KITAJIMA Masaki
Department of Surgery, Keio University School of Medicine, 35 Shinanomachi, Shinjuku-ku, Tokyo 160-8582, Japan; Department of Surgery, Tokyo Denryoku Hospital, 9-2 Shinanomachi, Shinjuku-ku, Tokyo 160-0016, Japan
Journal: Oncogene : (Basingstoke), 2002, 21 (5) 789-797
ISSN: 0950-9232 Availability: INIST-21693; 354000101291050100
No. of Refs.: 30 ref.
Document Type: P (Serial) ; A (Analytic)
Country of Publication: United Kingdom
Language: English
Restriction landmark genomic scanning (RLGS) was utilized to identify novel genomic alterations in hepatocellular carcinoma (HCC). Thirty-one HCC samples were examined by RLGS. Two high intensity spots were common to several RLGS profiles of different HCCs. Nucleotide sequencing and homology search analysis showed that these spots represented repetitive sequences, Human tandem repeat sequence (Genbank, L09552) and centromeric NotI cluster (Genbank, Y10752). These intensified signals were attributable to the occurrence of demethylated areas in the recognition sequence of the NotI site of the corresponding fragments. The intensity of these spots in the RLGS profile reflects their degree of demethylation, which was significantly correlated with postoperative recurrence, even in patients regarded as belonging to the good prognosis group by conventional prognostic factors. Multivariate analysis showed that the intensities of the two spots retained independent prognostic value. This is a new type of predictive factor for HCC based on epigenetic changes in hepatocarcinogenesis, and in the future it is expected to be of great value in making preoperative diagnosis and selecting postoperative therapy.

8/7/5 (Item 2 from file: 144)
DIALOG(R)File 144:Pascal

14586173 PASCAL No.: 00-0253650
A new predictive factor for hepatocellular carcinoma based on two-dimensional electrophoresis of genomic DNA
ITANO O; UEDA M; KIKUCHI K; SHIMAZU M; KITAGAWA Y; AIURA K; KITAJIMA M
Department of Surgery, Keio University School of Medicine, 35 Shinanomachi, Shinjuku-ku, Tokyo 160-8582, Japan; Department of Surgery. Tokyo Denryoku Hospital, 9-2 Shinanomachi, Shinjuku-ku, Tokyo 160-0016, Japan
Journal: Oncogene : (Basingstoke), 2000, 19 (13) 1676-1683
ISSN: 0950-9232 Availability: INIST-21693; 354000087115910070
No. of Refs.: 27 ref.
Document Type: P (Serial) ; A (Analytic)
Country of Publication: United Kingdom

Language: English

Molecular genetic analyses have clarified that accumulation of genomic changes provides important steps in carcinogenesis and have identified a number of valuable genetic markers for certain cancers. To date, however, no prognostic markers have been identified for hepatocellular carcinoma (HCC). In this study, we used restriction landmark genomic scanning (RLGS), a new high-speed screening method for multiple genomic changes, to detect unknown genetic alterations in HCC. Thirty-one HCC samples and their normal counterparts were examined by RLGS. Eight spot changes were common in several cases, and all were seen only on the HCC profile. Five of these spots were detected in more than 12 of 31 cases (38.7%). Viral infection had no influence on changes in the RLGS spots. The disease-free survival rate for patients with >= 16 changed RLGS spots was significantly lower than that for patients with fewer changed RLGS spots (<= 15 spots) (P<0.001). In multivariate analysis, the number of changed spots was proven to retain an independent prognostic value (relative risk 1.095: P=0.0031). These results suggest that the number of changed RLGS spots may be a useful biological marker for recurrence of HCC.

8/7/6 (Item 3 from file: 144)
DIALOG(R)File 144:Pascal

14078494 PASCAL No.: 99-0271277

DNA alterations in human oral squamous cell carcinomas detected by restriction landmark genomic scanning

YAMAMOTO K; KONISHI N; INUI T; NAKAMURA M; HIASA Y; KIRITA T; SUGIMURA M

Second Department of Pathology, Nara Medical University, Nara, Japan; Department of Oral and Maxillofacial Surgery, Nara Medical University, Nara, Japan

Journal: Journal of oral pathology & medicine, 1999, 28 (3) 102-106
ISSN: 0904-2512 Availability: INIST-15681; 354000083781690020
No. of Refs.: 23 ref.
Document Type: P (Serial) ; A (Analytic)
Country of Publication: Denmark
Language: English

Genetic abnormalities in human oral squamous cell carcinomas (OSCC) were examined using restriction landmark genomic scanning (RLGS), a method of two-dimensional gel analysis allowing detection of amplifications and other aberrations in genomic DNA. DNAs from 11 oral tumours as well as from contiguous normal squamous epithelium, were cleaved with the restriction enzyme Not I, (SUP 3 SUP 2 P) end-labeled and electrophoretically size-fractionated. Following a second digestion employing Hinf I, the further fragmented DNA was again electrophoretically separated. Five fragments/spots were found amplified in at least 64% (7/11) (chromosome nos. 4, 9-12 or 22) of carcinomas, with one of these spots amplified in 100(chromosome no. 4) of tumour samples. In addition, six other spots were frequently reduced in at least 55(chromosome nos. 15 or 9-12) of tumour tissues. Further characterization of these common changes is needed to determine if they represent important alterations in OSCC.

8/7/7 (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

11069605 21077521 PMID: 11210171

Aberrant methylation of genes in low-grade astrocytomas.

Costello J F; Plass C; Cavenee W K

University of California-San Francisco, The Brain Tumor Research Center,

USA. jcostello@cc.ucsf.edu
Brain tumor pathology (Japan) 2000, 17 (2) p49-56, ISSN 1433-7398
Journal Code: 9716507
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
The underlying basis of the **malignant** progression of astrocytomas is a specific and cumulative series of genetic alterations, most of which are confined to high-grade tumors. In contrast, a proportion of low-grade astrocytomas have a relatively normal-appearing genome when examined with standard genetic screening methods. These methods do not detect epigenetic events such as aberrant methylation of CpG island, which result in transcriptional silencing of important cancer genes. To determine if aberrant methylation is involved in the early stages of astrocytoma development, we assessed the methylation status of 1,184 genes in each of 14 low-grade astrocytomas using **restriction landmark genome scanning** (RLGS). The results showed nonrandom and astrocytoma-specific patterns of aberrantly methylated genes. We estimate that an average of 1,544 CpG island-associated genes (range, 38 to 3,731) of the approximately 45,000 in the genome are aberrantly methylated in each tumor. Expression of a significant proportion of the genes could be reactivated by 5-aza-2-deoxycytidine-induced demethylation in cultured glioma cell lines. The data suggest that aberrant methylation of genes is more prevalent than genetic alterations and may have consequences for the development of low-grade astrocytomas.
Record Date Created: 20010207
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3694041 INSIDE CONFERENCE ITEM ID: CN038873647

Aberrant methylation of genes in low-grade **astrocytomas**

Costello, J. F.; Plass, C.; Cavenee, W. K.

CONFERENCE: International symposium of brain tumor pathology-2nd
BRAIN TUMOR PATHOLOGY, 2000; VOL 17; NO 2 P: 49-56
Springer, 2000
ISSN: 1433-7398
LANGUAGE: English DOCUMENT TYPE: Conference Selected papers
CONFERENCE SPONSOR: Japan Society of Brain Tumor Pathology
CONFERENCE LOCATION: Nagoya, Japan 2000; May (200005) (200005)
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Also known as ISBTP. Held in conjunction with the 18th annual meeting of the Japan Society of Brain Tumor Pathology; See also 5021.650 vol 49 no 2 2000 for abstracts